

**REMARKS**

Reconsideration is requested.

The specification has been amended to include a cross-reference to the parent applications, as suggested by the Examiner.

The specification has been amended to include a reference to the Brief Description of the Drawings. The description of Figure 6 has also been amended to obviate the objection to the disclosure. Nothing further is believed to be required in this regard however the Examiner is requested to advise the undersigned if otherwise.

The Examiner is requested to return a completely initialed PTO-1449 Form which was filed October 18, 2001, as a partially initialed copy of the same was received with the Office Action of June 30, 2004. Specifically, the Examiner has initialed all the references except for U.S. Patent No. 5,650,298 and executed the entirety of the PTO-1449 Form. The Examiner has cited U.S. Patent No. 5,650,298, in rejecting the claims of the application such that the undersigned presumes the Examiner has considered the reference and a completely initialed copy of the PTO-1449 Form bearing the OIPE stamp of January 2, 2002, is requested. The undersigned further notes that the Examiner has listed the patent on the PTO-892 Form received with the Office Action of June 30, 2004.

The specification has been amended to include sequence identifiers and a revised Sequence Listing to include the sequences disclosed on page 35 of the application, as required by the Examiner. The attached paper and computer readable copies of the Sequence Listing are the same. No new matter has been added.

The specification is submitted to be in compliance with the Rules however the Examiner is requested to advise the undersigned in the event anything further is required.

The claims have been amended with the Examiner's comments on page 4 of the Office Action dated June 30, 2004, in mind. Withdrawal of the objections of the claims is requested.

The Section 112, second paragraph, rejection of claims 1-4, 9 and 15 is moot in view of the above. The pending claims are submitted to be definite.

The Section 102 rejection of claims 1-4 over Bujard (U.S. Patent No. 5,650,298) is moot in view of the above. The claims are submitted to be patentable over the cited art and consideration of the following in this regard is requested.

The '298 patent is believed to relate to transgenic animals presenting two transgenes; one of which codes for tTA and the other for a polypeptide under control of a promoter containing the operators tet. This document also relates to constructions for targeted introduction by homologous recombination of the transgene coding for the transactivator tTA.

The '298 document describes two different embodiments which the applicants believe must be considered separately. In a first embodiment, this document describes particular constructions intended to allow the integration of a tetracycline-regulated expression system in a specific region of the genome of a cell. These constructions comprise in particular sequences of homologies to allow the homologous recombination. Thus, as specified in claim 11 of '298, the DNA molecule comprises a sequence of a 5' flanking regulatory region of the gene of interest. This region must be

sufficiently large to allow the homologous recombination (see col. 3, lines 34-42). The '298 patent does not specify nor suggest that the sequence of a 5' flanking regulatory region must be functional in the targeting construct intended to allow the integration of a tetracycline-regulated expression system and that this sequence includes the promoter of the gene of interest. On the contrary, the applicants believe that it is specified in '298 patent (col 14 l. 36-41) that the presence of the promoter region of the gene of interest in the targeting construct is completely excluded. FIG 13 shows the targeting construct integrated into the genome.

In the second embodiment disclosed in the '298 patent, the applicants believe that two separate and distinct constructs are used: a first one carries the sequence coding for the transactivator tTA; the other carries a promoter linked to tet operators and a coding sequence (see FIG 11). Thus, this embodiment is clearly different from the object of the present invention. Moreover, the promoter of the  $\beta$ -actin has been described in the '298 patent only within this second embodiment.

The '298 patent therefore is not believed to teach the presently claimed invention.

The Section 102 rejection of Claim 15 over Jackerott (Journal of Histochem. & Cytochem. 1997; 45(12):1643-50), is moot in view of the above. The claims are submitted to be patentable over the cited art and consideration of the following in this regard is requested.

Claims 15 has been rewritten as new claim 34. Claim 34 is directed to an isolated cell comprising a recombinant adenovirus which comprises a nucleic acid according to claim 9. The claimed isolated nerve cell is not disclosed nor suggested by Jackerott et al.

MALLET et al  
Appl. No. 09/831,335  
September 30, 2004

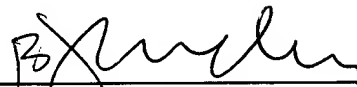
The present application is submitted to be in condition for allowance and a Notice to that effect is requested.

The Examiner is requested to advise the undersigned in the event anything further is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_

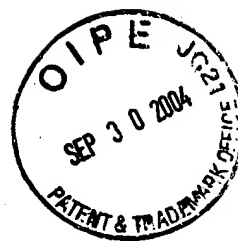
A handwritten signature in black ink, appearing to read "B. J. Sadoff", written over a horizontal line.

B. J. Sadoff  
Reg. No. 36,663

BJS:  
1100 North Glebe Road, 8th Floor  
Arlington, VA 22201-4714  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100



## SEQUENCE LISTING



<110> MALLET, JACQUES  
CORTI, OLGA

<120> NOVEL SYSTEM FOR REGULATING TRANSGENE EXPRESSION

<130> 3665-94

<140> PCT/FR99/02752

<141> 1999-11-09

<150> FR9814080

<151> 1998-11-09

<150> US/122600

<151> 1999-03-03

<160> 3

<170> PatentIn Ver. 2.1

<210> 1

<211> 2502

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of artificial sequence: Regulation Sequence

<400> 1

```
ctcaggagc tcgaattcat atgtctagat tagataaaag taaagtgatt aacagcgcac 60
tagagctgct taatgaggct ggaatcgaag gtttaacaac ccgtaaactc gcccagaagc 120
taggtgtaga gcagcctaca ttgtattggc atgtaaaaaa taagcgggct ttgctcgacg 180
ccttagccat tgagatgtta gataggcacc atactcactt ttgcccttta gaaggggaaa 240
gctggcaaga ttttttacgt aataacgcta aaagtttttag atgtgcttta ctaagtcac 300
gcgatggagc aaaagtacat ttaggtacac ggcctacaga aaaacagtat gaaactctcg 360
aaaatcaatt agccttttta tgccaacaag gtttttctact agagaatgca ttatatgcac 420
tcagcgtgtg ggggcatttt actttagggt gcgtattgga agatcaagag catcaagtcg 480
ctaaagaaga aagggaaaca cctactactg atagtatgcc gccattatta cgacaagcta 540
tcgaattatt tgatcaccaa ggtgcagagc cagccttctt attcggcctt gaattgatca 600
tatgctggatt agaaaaacaa cttaaattgtg aaagtgggtc cgcgtacagc cgcgcgcgta 660
cgaaaaacaa ttacgggtct accatcgagg gcctgctcga tctcccggac gacgacgcc 720
ccgaagaggc ggggctggcg gctccgcgcc tgtcctttct ccccgcgga cacacgcgca 780
gactgtcgac ggcccccccg accgatgtca gcctggggga cgagctccac ttagacggcg 840
aggacgtggc gatggcgcat gccgacgcgc tagacgattt cgatctggac atgttggggg 900
acggggattc cccgggtccg ggatttacc cccacgactc cgccccctac ggcgctctgg 960
atatggccga cttcgagttt gagcagatgt ttaccgatgc ctttgaatt gacgagtacg 1020
gtgggtaggg ggcgcgagga tctcagattt gtgcatacac agtgactcat actttcacca 1080
atactttgca ttttgataa atactagaca actttagaag tgaattattt atgaggttgt 1140
cttaaaatta aaaattacaa agtaataaat cacattgtaa tgtattttgt gtgataccca 1200
gaggtttaag gcaacctatt actcttatgc tcctgaagtc cacaattcac agtcctgaac 1260
tataatctta tctttgtgat tgctgagcaa atttgcagta taatttcagt gcttttaaat 1320
tttgtcctgc ttactatttt ctttttttat ttgggtttga tatgctgca cagaatgggg 1380
cttctattaa aatattccat ggcttacatt tttaatgttt tgttctctta atatgttcaa 1440
agctactcaa cttttattcc cgaaaaatgt ttactttaat tattctaatt tcttacataa 1500
agcattgagg tgctaacaat tatatactat gtacaagatg gcagactaaa tcatatcata 1560
```

```

ccatcaagta gaaacctgga gtttggtgaa ctttgagttg tttatatgtc tctcctttat 1620
tgtcttctca aaacctgtga ttctgaagtc aaagggacac agctgtcaca tgaaaagtga 1680
tcacttatca cctgtatgcy taaaacacct taccaagcag ctaagaggag taactcctag 1740
ccactttgag aaacgttttt gaataaacag agcaaggctc ttccccattc tcccagagat 1800
atagcataaa actgagcgca tttttataaa acaaaaaagg aggaatgtgt ggtttgatgg 1860
ccagaccctg aattttgagtt cagcatctgc ttttccatat tatagatggg taccagtgat 1920
tctgagccat gtctatttct cctgactttt cctctgtttt cccacgcttg ctgatattta 1980
cagccgtggt catcacaatc acctttgttc ctttcttcct tcctccaact ctgcattaaa 2040
ttccaggaaac ttgcttttctg tgaagtctga gtttaccact ccctatcagt gatagagaaa 2100
agtgaaagtc gagtttacca ctccctatca gtgatagaga aaagtgaaag tcgagtttac 2160
cactccctat cagtgataga gaaaagtga agtcgagttt accactccct atcagtgata 2220
gagaaaagtg aaagtcgagt ttaccactcc ctatcagtga tagagaaaag tgaaagtcga 2280
gtttaccact ccctatcagt gatagagaaa agtgaaagtc gagtttacca ctccctatca 2340
gtgatagaga aaagtgaaag tcgagctcgg taccggggtc gagtaggcgt gtacgggtggg 2400
aggcctatat aagcagagct cgtttagtga accgtcagat cgcctggaga cgccatccac 2460
gctgttttga cctccataga agacaccggg accgatccag cc 2502

```

<210> 2

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of artificial sequence: alu primer

<400> 2

ttgcagtgag ccgagatcgc gcc

23

<210> 3

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of artificial sequence: exon1 oligonucleotide

<400> 3

tgctgtcttg gcgtccagct cagaca

26